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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/579,369

05/15/2006

Jeffry B. Stock

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EXAMINER

GITOMER, RALPH J

ART UNIT

PAPER NUMBER

1657

MAIL DATE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/579,369	<b>Applicant(s)</b> STOCK ET AL.	
	<b>Examiner</b> Ralph Gitomer	<b>Art Unit</b> 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 12-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>1/29/07</u> . | 6) <input type="checkbox"/> Other: _____  |

Applicant's election without traverse of Group I, claims 1-11, in the reply filed on 5/19/08 is acknowledged. The IDS received 1/29/07 has been considered.

Although not claimed, the point of novelty may reside in the connection between PP2A phosphatase activity which can be modulated by methylation and the degree of phosphorylation of tau by PP2A depending upon the activity of PP2A. However, this has not been clearly set forth in the specification as filed nor its figures.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee.

Lee (PNAS) entitled "A Specific Protein Carboxyl Methyltransferase That Demethylates Phosphoprotein Phosphatase 2A in Bovine Brain" teaches on page 6044 column 1 last full paragraph, identifying a compound that is responsible for demethylation of PP2A is described. On page 6046 Fig. 4 shows inhibition of demethylation reaction of PP2A by a compound identified.

All the features of the claims are taught by Lee for the same function as claimed.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4, 5, 10, 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Lee in view of Roder.

See the teachings of Lee above.

The claims differ from Lee in that they specify the protein activity is phosphorylation of tau which is hyperphosphorylated and the compound modulates methylation of PP2A and thereby decreases tau hyperphosphorylation.

Roder (6,541,468) entitled "Indolocarbazole Derivatives Useful for the Treatment of Neurodegenerative Diseases and Cancer" teaches in column 1 lines 49-54, it is desirable to have a pharmaceutical means to interfere with the pathological process of tau hyperphosphorylation. In column 2 first paragraph the most convincing cellular models involve PP2A inhibition.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modulate the activity of PP2A by demethylating the enzyme as taught by Lee and thereby reduce hyperphosphorylation of tau because Roder teaches the relationship between PP2A activity and pathological tau hyperphosphorylation. Further, modulating the activity of PP2A by any means, such as methylation as taught by Lee, would then inherently change the tau phosphorylation. No new pathways are taught.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to identifying a compound for altering a protein activity. There are a number of assays disclosed in the specification as originally filed and substances administered to mice to alter a protein activity. However, no compounds are disclosed that alter a protein activity and none are identified by any assay.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while disclosing identifying compounds that increase methylation of PP2A phosphatase specifically in order to reduce hyperphosphorylation of tau, does not reasonably provide enablement for “altering a protein activity”, “a protein activity”, “a phosphorylated protein”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In claim 1 and all occurrences, the terms “altering a protein activity”, “a protein activity”, “a phosphorylated protein” lack enablement as it would require one of ordinary skill in this art undue experimentation to determine which such activity or protein would work in the instant invention.

The entire scope of the claims has not been enabled because:

1. Quantity of experimentation necessary would be undue because of the large proportion of inoperative activities and proteins claimed.
2. Amount of direction or guidance presented is insufficient to predict which activities or proteins encompassed by the claims would work.
3. Presence of working examples are only for single specific substances and extension to other compounds has not been specifically taught or suggested.
4. The nature of the invention is complex and unpredictable.
5. State of the prior art indicates that most related proteins or activities are not effective for the claimed functions.
6. Level of predictability of the art is very unpredictable.

7. Breadth of the claims encompasses an innumerable number of proteins and activities.

8. The level of one of ordinary skill in this art is variable.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

The independent claims are incomplete where they are directed to identifying a compound but lack any such steps. How the claimed steps are performed is not set forth. What compounds react with what and what is determined have not been set forth. In claims 7 and 8, “an extract of a natural product” and “an extract of a traditional medicine” are meaningless and read on water to air.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Stock (2006/0171938 A1) teaches compositions that increase the level of methylation of PP2A.

Beachy (6,277,566) teaches compounds that modulate PP2A phosphatase.

Mandelkow (6,200,768) teaches treating AD with PP2A.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (571) 272-0916. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ralph Gitomer/  
Primary Examiner, Art Unit 1657

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Primary Examiner  
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